



CTMM DeCoDe

translational research on colorectal cancer in the Netherlands

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Facts & figures

- Netherlands
- AKA Holland
- 40.000 km²
- 17 million people
- 8 UMC's







Dutch Daily News

Saturday, June 19,

[Home](#) [News](#) [Features](#) [International](#) [Business](#) [Entertainment](#) [Technology](#) [Health](#) [Travel](#)

FIFA bans Dutch babes in orange mini-dress from World Cup





Fixtures and Results

| | | | |
|-----------|-----|--------------------|-----|
| 14 Jun 10 | NED | 2:0 (0:0) » | DEN |
| 14 Jun 10 | JPN | 1:0 (1:0) » | CMR |
| 19 Jun 10 | NED | 1:0 (0:0) » | JPN |
| 19 Jun 10 | CMR | 1:2 (1:1) » | DEN |
| 24 Jun 10 | DEN | Background | JPN |
| 24 Jun 10 | CMR | Background | NED |

[More »](#)

Standings

| | MP | W | D | L | Pts |
|-------------|----|---|---|---|-----|
| Netherlands | 2 | 2 | 0 | 0 | 6 |
| Japan | 2 | 1 | 0 | 1 | 3 |
| Denmark | 2 | 1 | 0 | 1 | 3 |
| Cameroon | 2 | 0 | 0 | 2 | 0 |

Translating biology to medicine



Translational Research Pipeline

U medisch centrum



Academia

Model systems

Biobanks

Clinical series

Multidisciplinary

marker
identification

marker
validation

assay
development

pilot
studies

cost
effectiveness

Implementation
studies

molecular
test

Industry

Technology

Automation

Upscaling

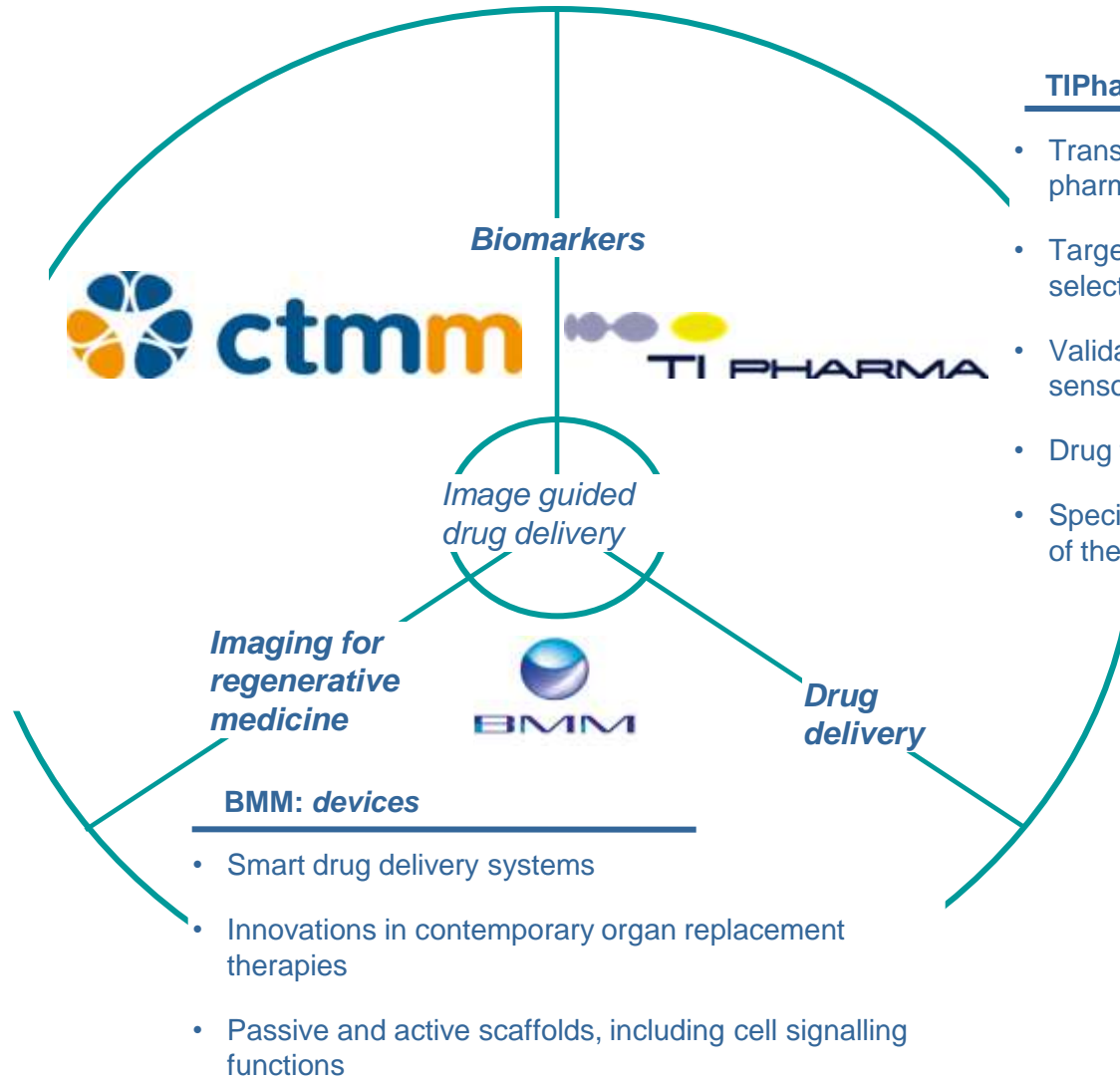
Valorisation



CTMM, TIPharma and BMM offer an integrated approach for innovations in the Dutch health care sector

CTMM: *diagnosis*

- Early detection of disease by in-vitro and in-vivo diagnostics
- Stratification of patients for personalized treatment
- Assessing efficiency and efficacy of medicines by imaging
- Image guided delivery of medication
- Focus on cancer, cardiovascular, neurodegenerative and infectious /autoimmune disease.



TIPharma: *drugs*

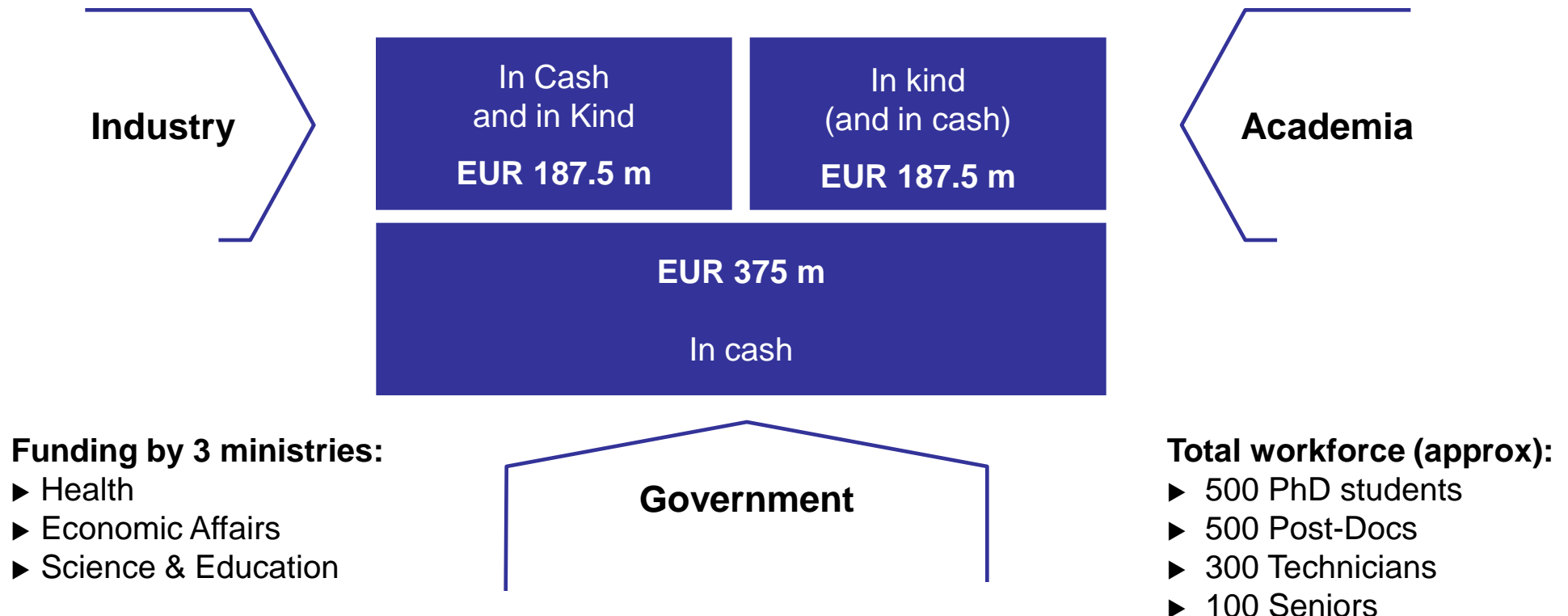
- Translational research on novel pharmaceutical therapies
- Target finding, animal models and lead selection
- Validation of biomarkers and bio-sensing
- Drug formulation, delivery and targeting
- Special Theme focusing on the efficiency of the process of drug development

BMM: *devices*

- Smart drug delivery systems
- Innovations in contemporary organ replacement therapies
- Passive and active scaffolds, including cell signalling functions

The Dutch model: financing by industry, academia & government

Total five year funding for CTMM, TI Pharma and BMM: EUR 750 million



CTMM

- multidisciplinary projects
 - Cancer
 - Cardiovascular disease
 - Inflammation
 - Neurodegenerative diseases
- ‘bench’ to ‘bedside’
- Financial contribution
 - government (50%)
 - academia (25%)
 - industry (25%)



Center for Translational
Molecular Medicine

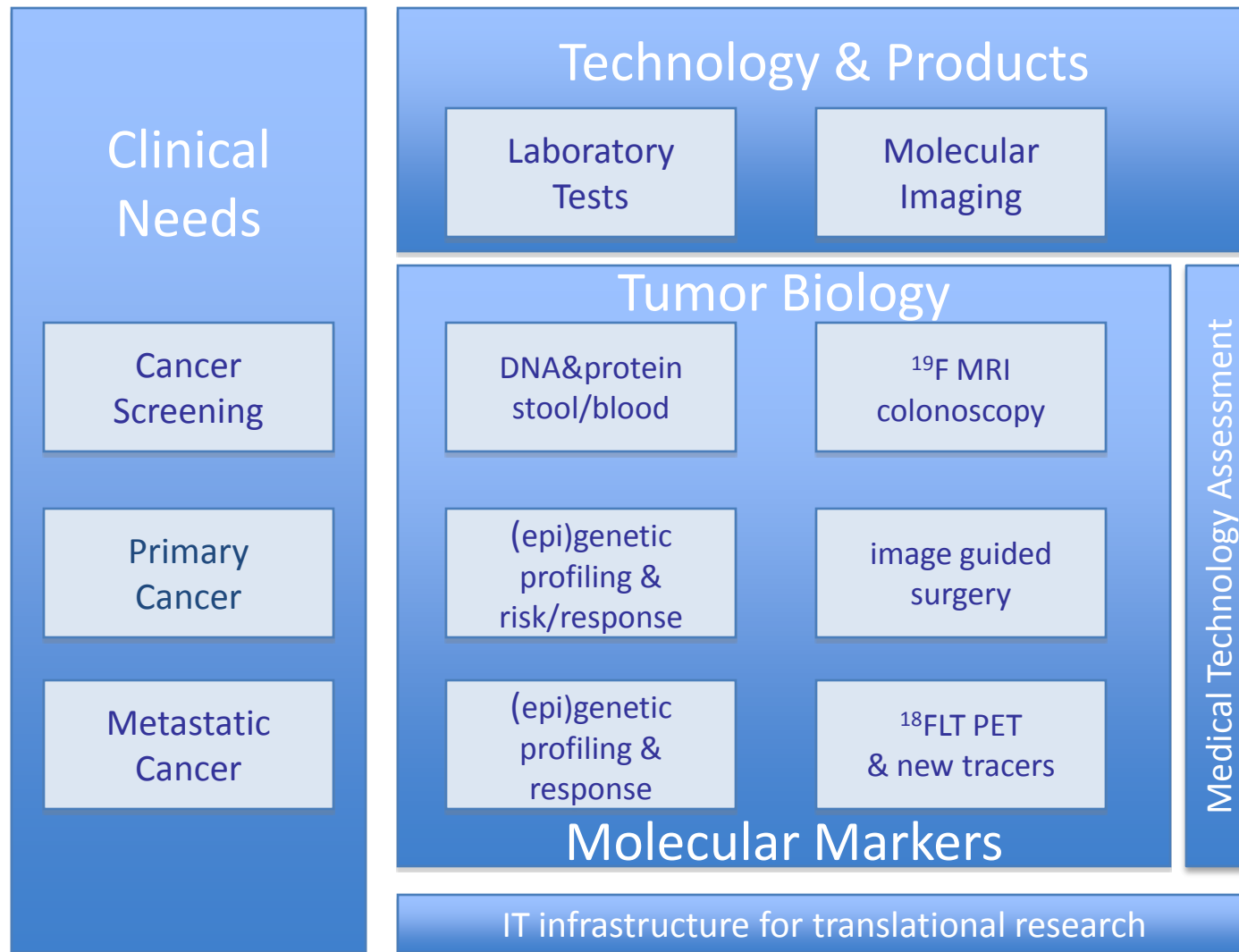
Translating science into better healthcare

DeCoDe

Decrease Colorectal cancer Death

PI: Gerrit Meijer

Decrease Colorectal cancer Death



DeCoDe partners



LU
MC
LEIDE UNIVERSITAIR MEDISCH CENTRUM

PERCUROS

ServiceXS

Erasmus MC
Universitair Medisch Centrum Rotterdam

PHILIPS
sense and simplicity

decode
a ctmm project

VU medisch centrum

OncoMethylome
SCIENCES

DIONEX

nipad

cyteltra

MRC-Holland
MLPA

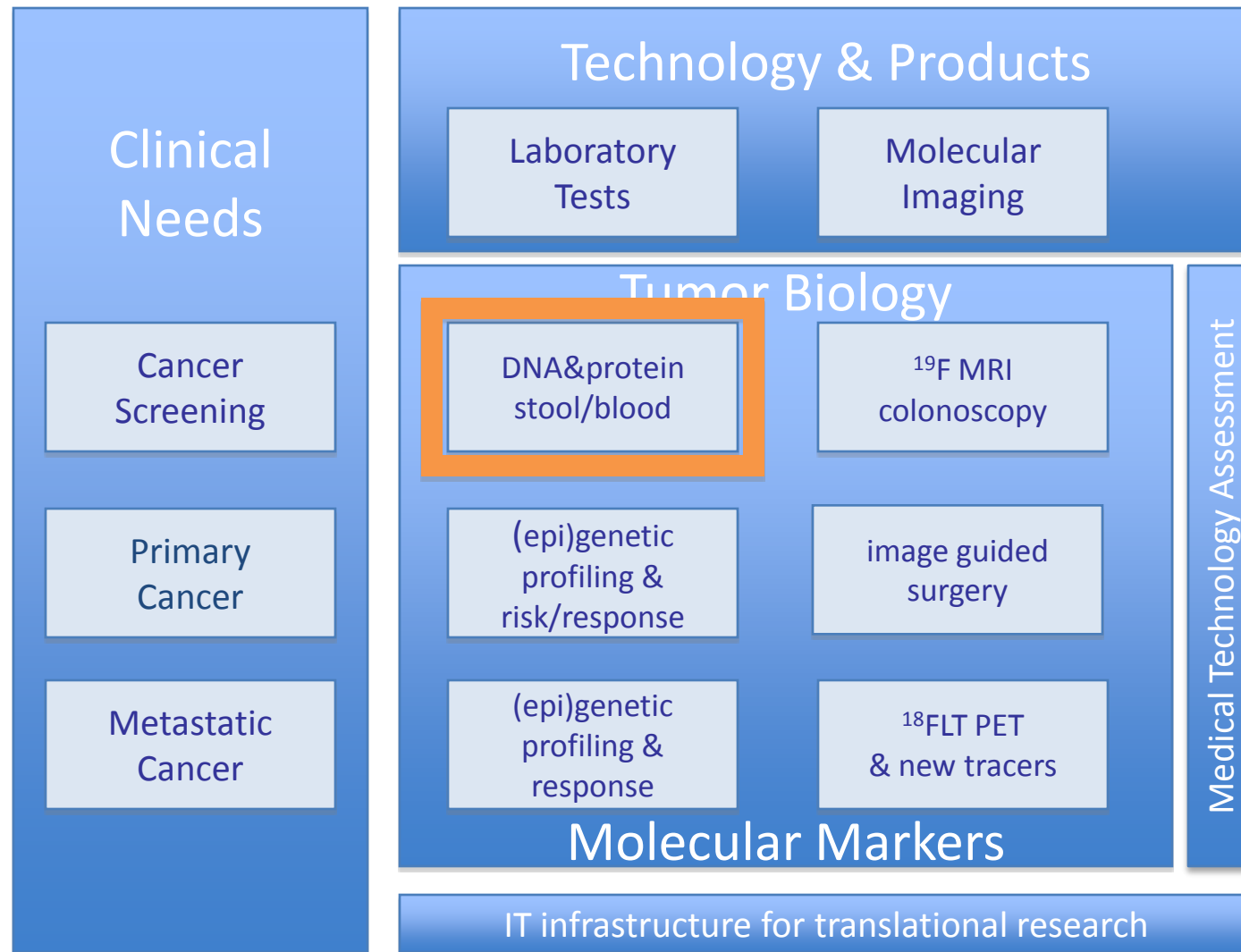
amC

Academisch Medisch Centrum
Universiteit van Maastricht

academisch ziekenhuis
Maastricht
azM

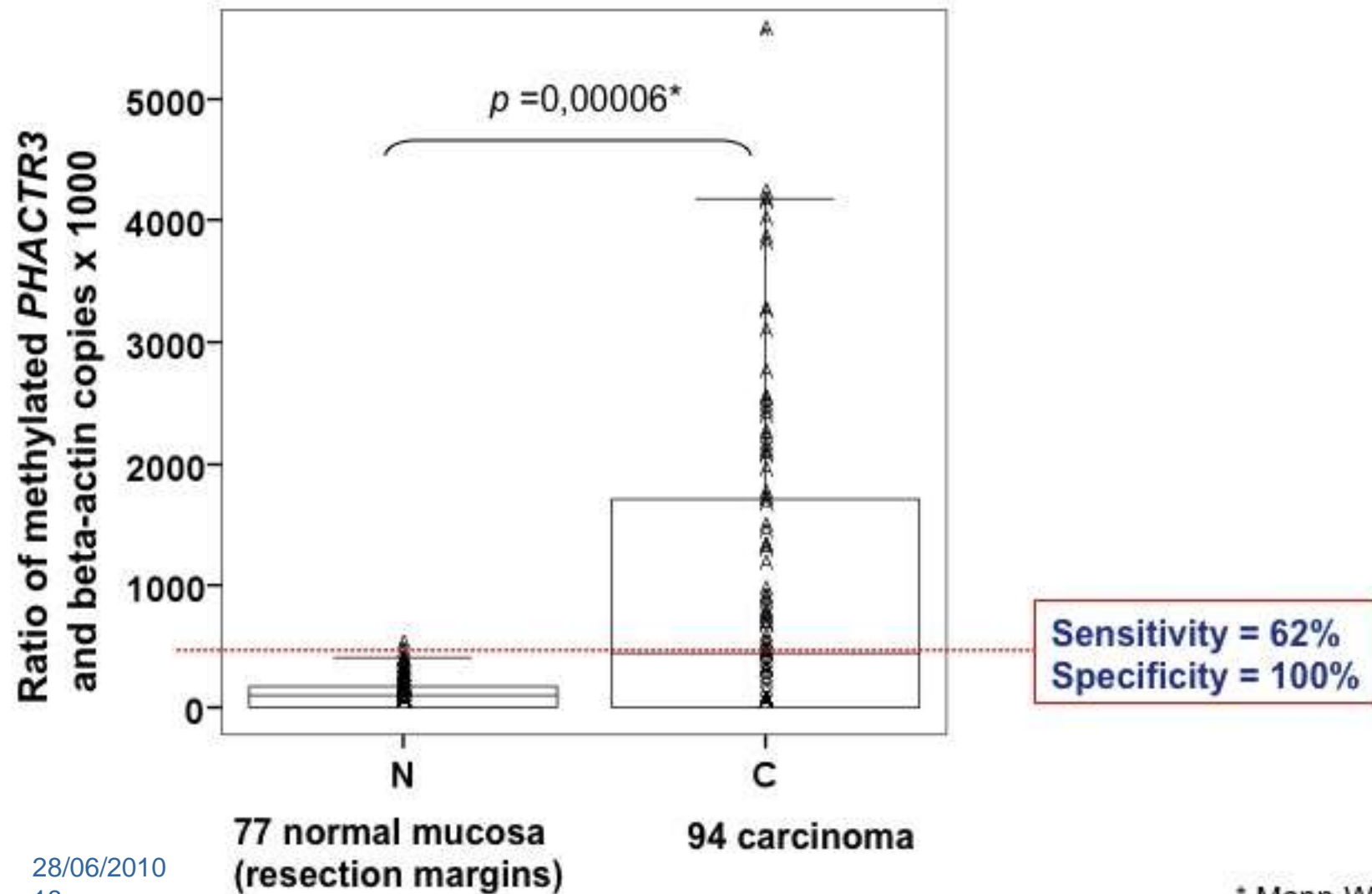
ctmm

Decrease Colorectal cancer Death





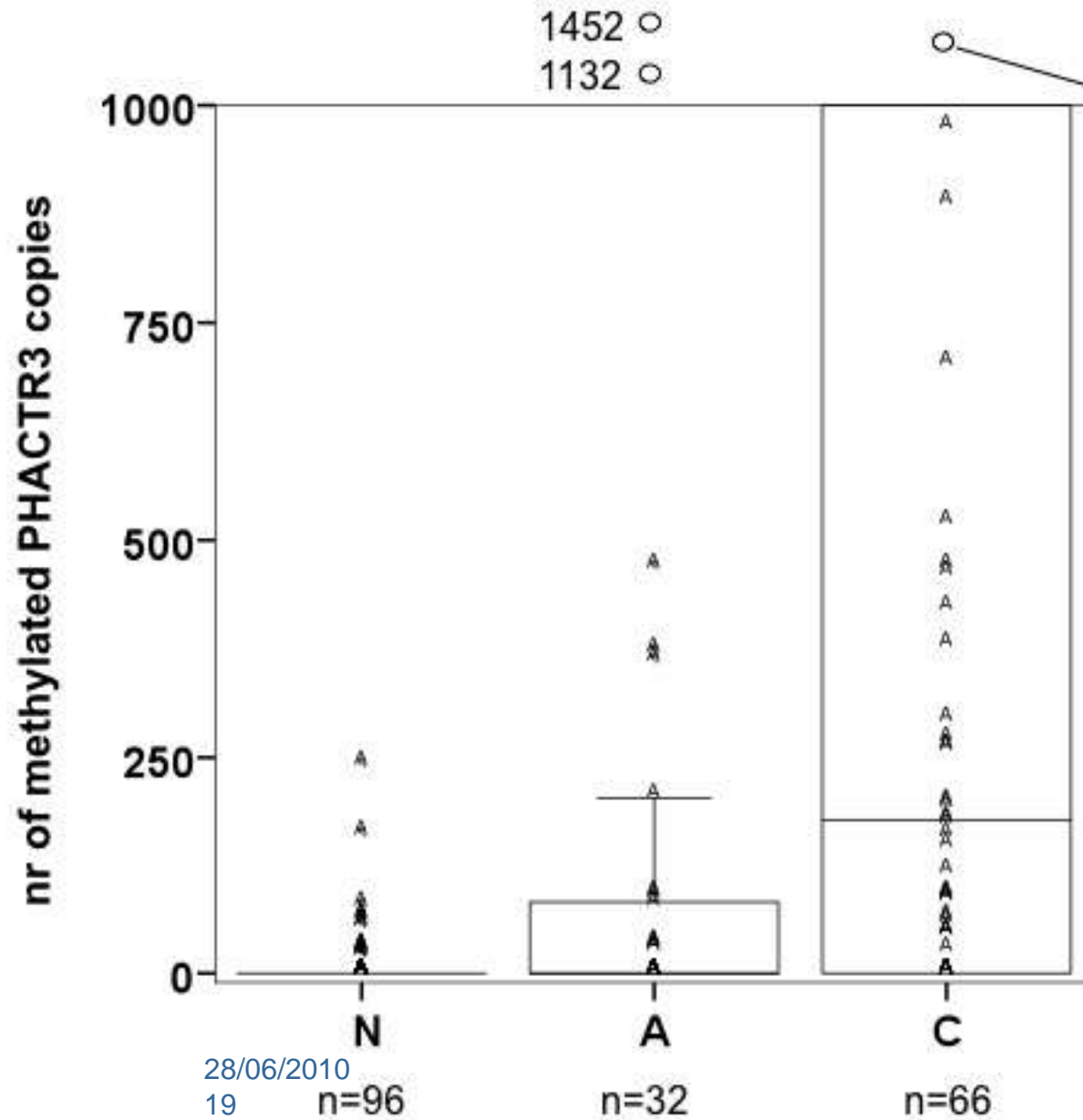
PHACTR3 methylation levels in tissue samples



28/06/2010
18

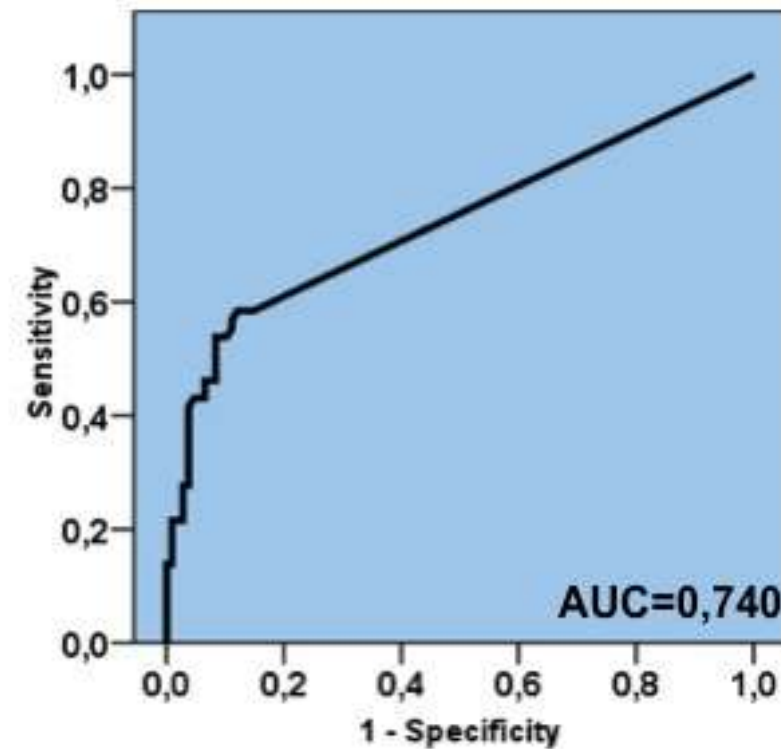
PHACTR3 methylation levels in stool samples

VU university medical center
Department of Pathology
Tumor Profiling Unit



18 data points
1500 – 32000 copies

AA and C



28/06/2010

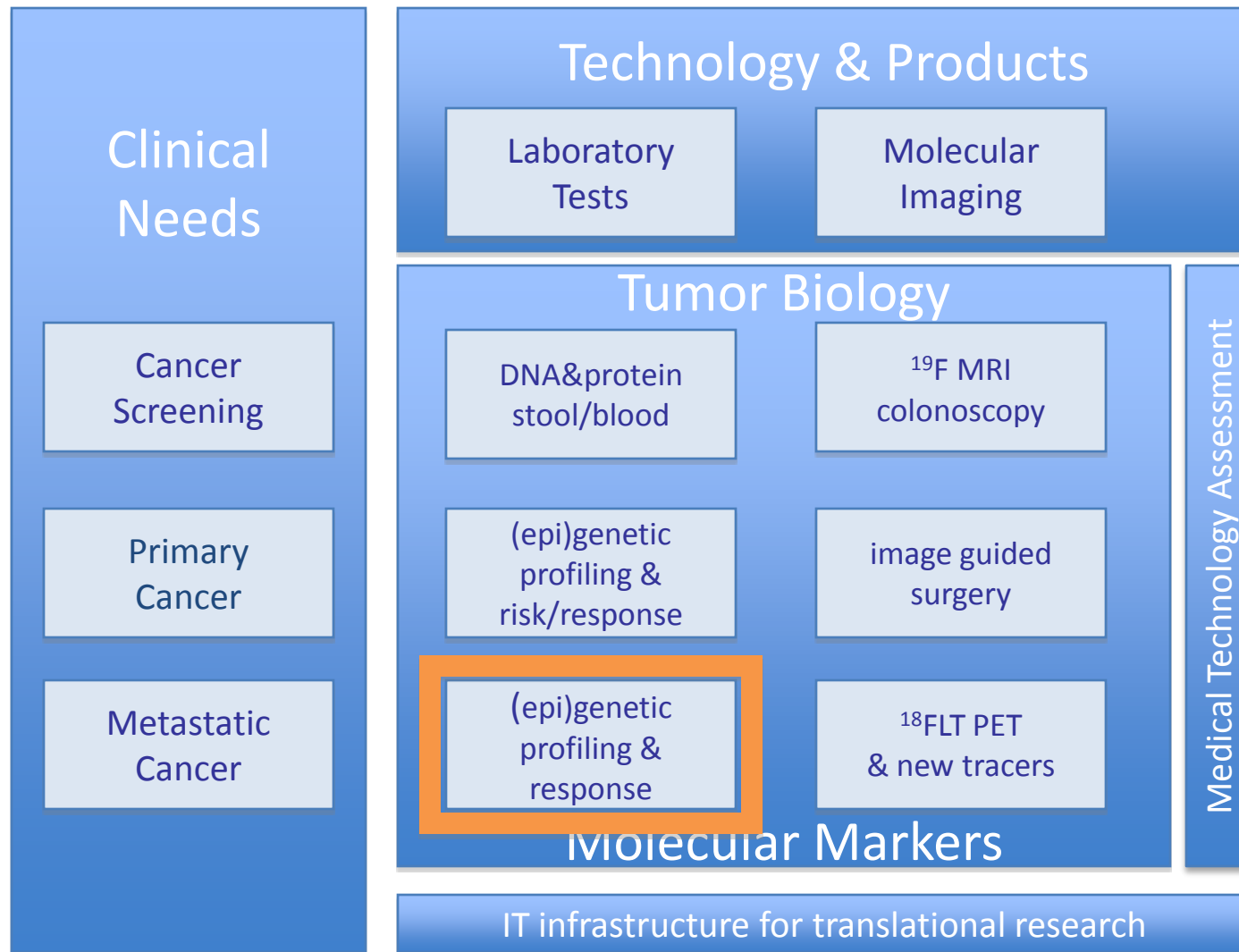
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Decrease Colorectal cancer Death

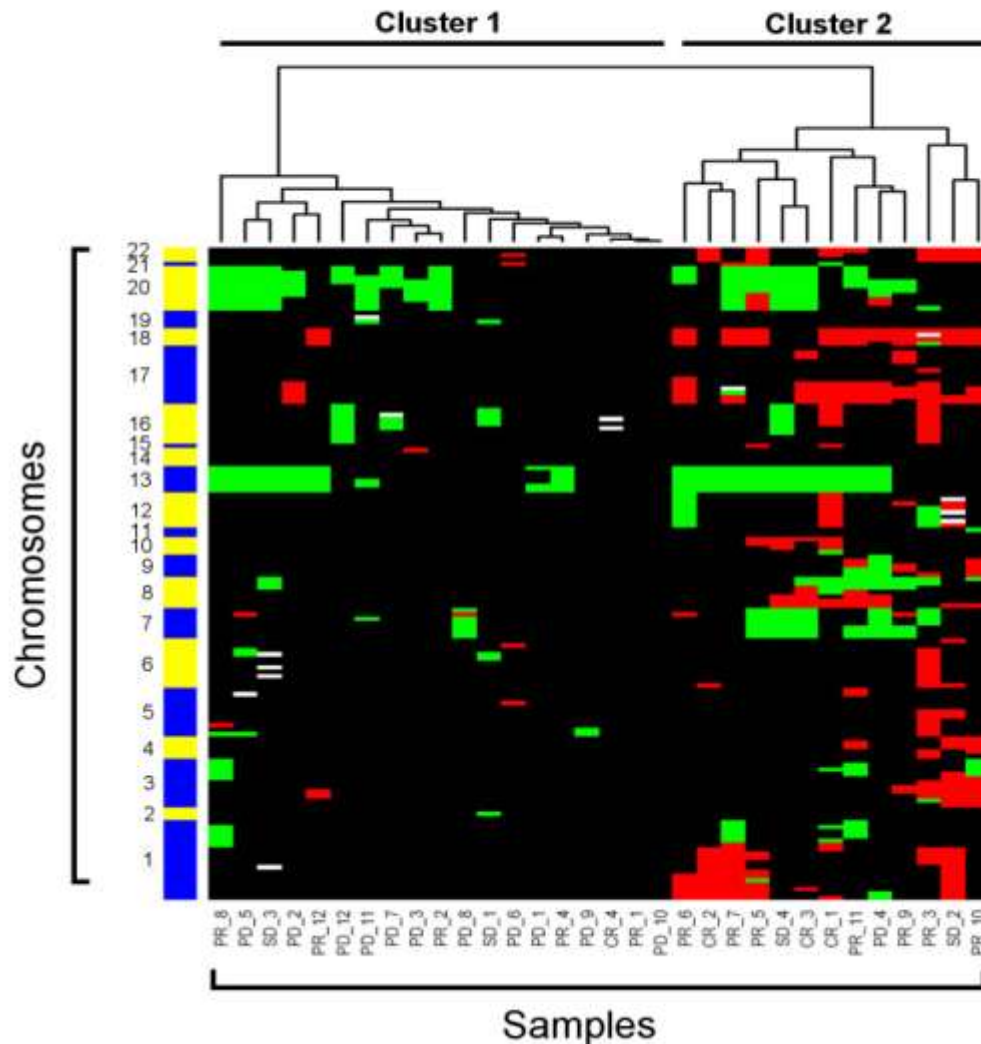
- Prospective validation
 - cohort study with gold standard test = colonoscopy
 - Screening population
 - Referral population
- Complex logistics
- Biobanking
- Data management



Decrease Colorectal cancer Death



Variation in DNA copy number profiles in CRC correlates to response to therapy



| | <i>Response</i> | <i>no response</i> | <i>total</i> |
|-----------|-----------------|--------------------|--------------|
| cluster 1 | 6 | 13 | 19 |
| cluster 2 | 10 | 3 | 13 |
| | 16 | 16 | 32 |
| | | $p = 0.03$ | |

Postma et al, Ann Oncol 2009

Sequential versus combination chemotherapy with capecitabine, irinotecan, and oxaliplatin in advanced colorectal cancer (CAIRO): a phase III randomised controlled trial

Miriam Koopman, Ninja F Antonini, Joep Douma, Jaap Wals, Aafke H Honkoop, Frans L G Erdkamp, Robert S de Jong, Cees J Rodenburg, Gerard Vreugdenhil, Olaf J L Loosveld, Aart van Bochove, Harm A M Sinnige, Geert-Jan M Creemers, Margot E T Tesselaar, Peter H Th J Slee, Marjon J B P Werter, Linda Mol, Otilia Dalesio, Cornelis J A Punt

Lancet 2007; 370: 135-42

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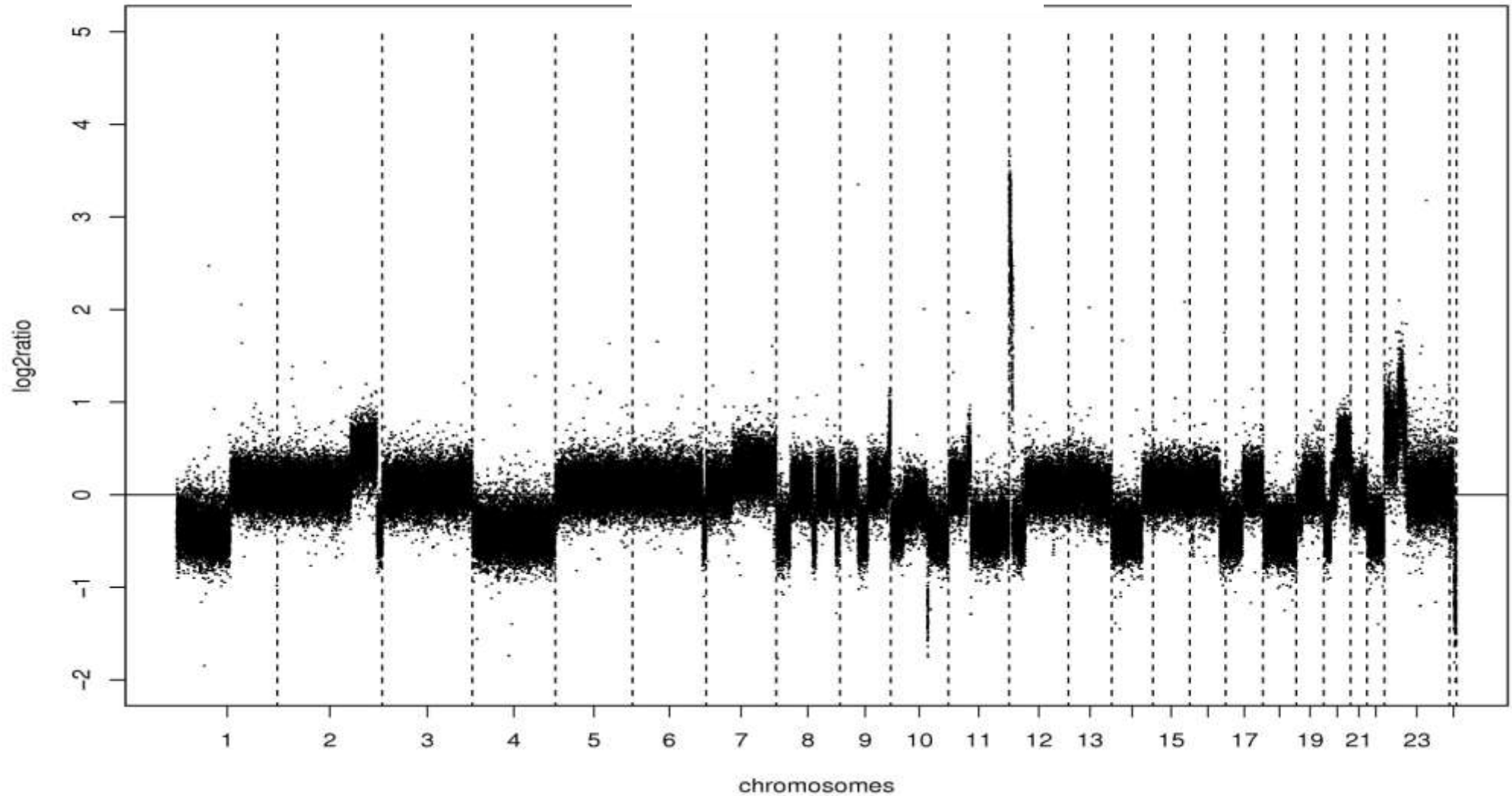
Chemotherapy, Bevacizumab, and Cetuximab in Metastatic Colorectal Cancer

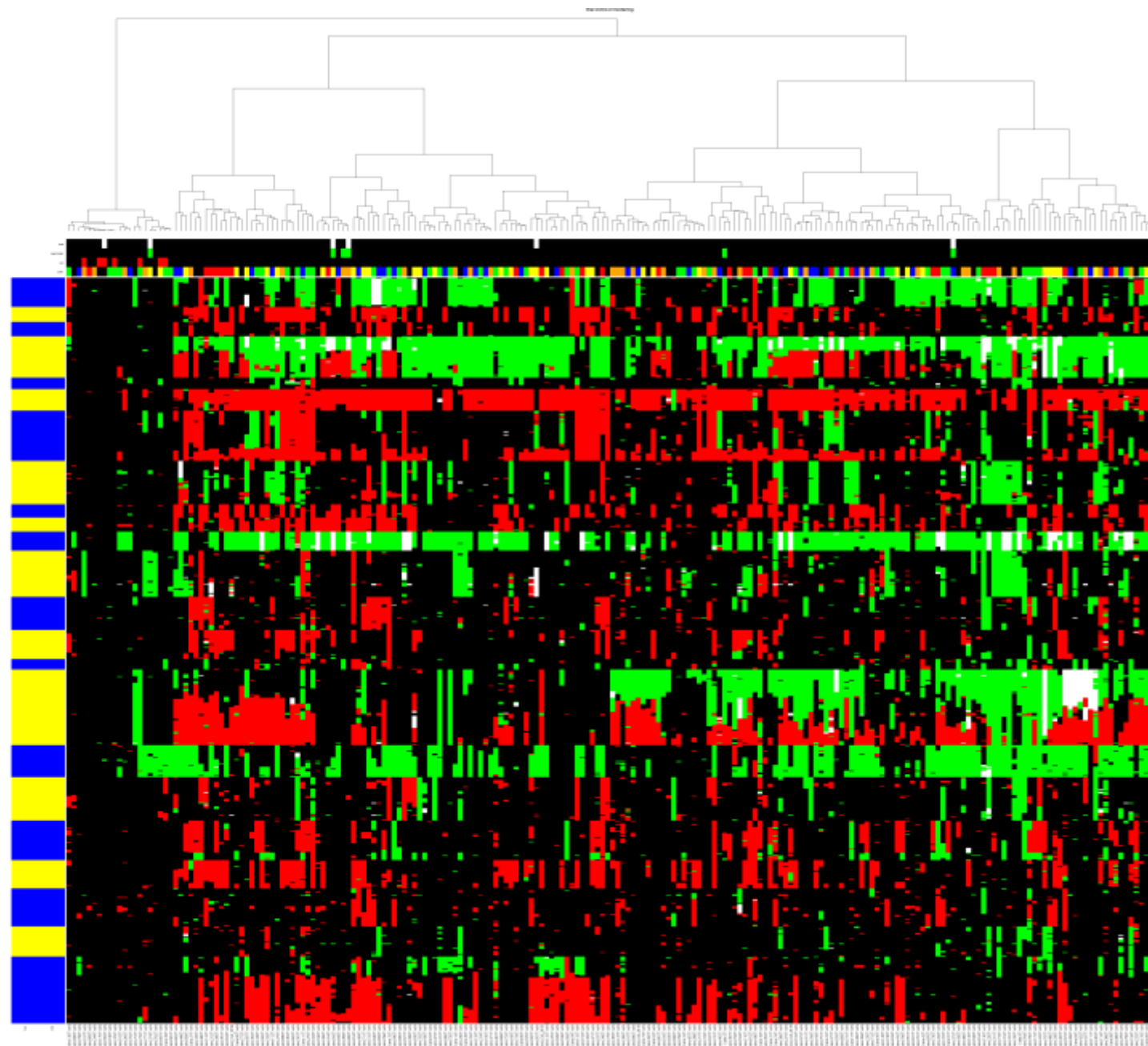
Jolien Tol, M.D., Miriam Koopman, M.D., Annemieke Cats, M.D., Ph.D., Cees J. Rodenburg, M.D., Ph.D.,
Geert J.M. Creemers, M.D., Ph.D., Jolanda G. Schrama, M.D., Frans L.G. Erdkamp, M.D., Ph.D.,
Allert H. Vos, M.D., Cees J. van Groeningen, M.D., Ph.D., Harm A.M. Sinnige, M.D., Ph.D.,
Dirk J. Richel, M.D., Ph.D., Emile E. Voest, M.D., Ph.D., Jeroen R. Dijkstra, B.Sc., Marianne E. Vink-Börger, M.Sc.,
Ninja F. Antonini, M.Sc., Linda Mol, M.Sc., Johan H.J.M. van Krieken, M.D., Ph.D., Otilia Dalesio, M.Sc.,
and Cornelis J.A. Punt, M.D., Ph.D.

Decrease Colorectal cancer Death

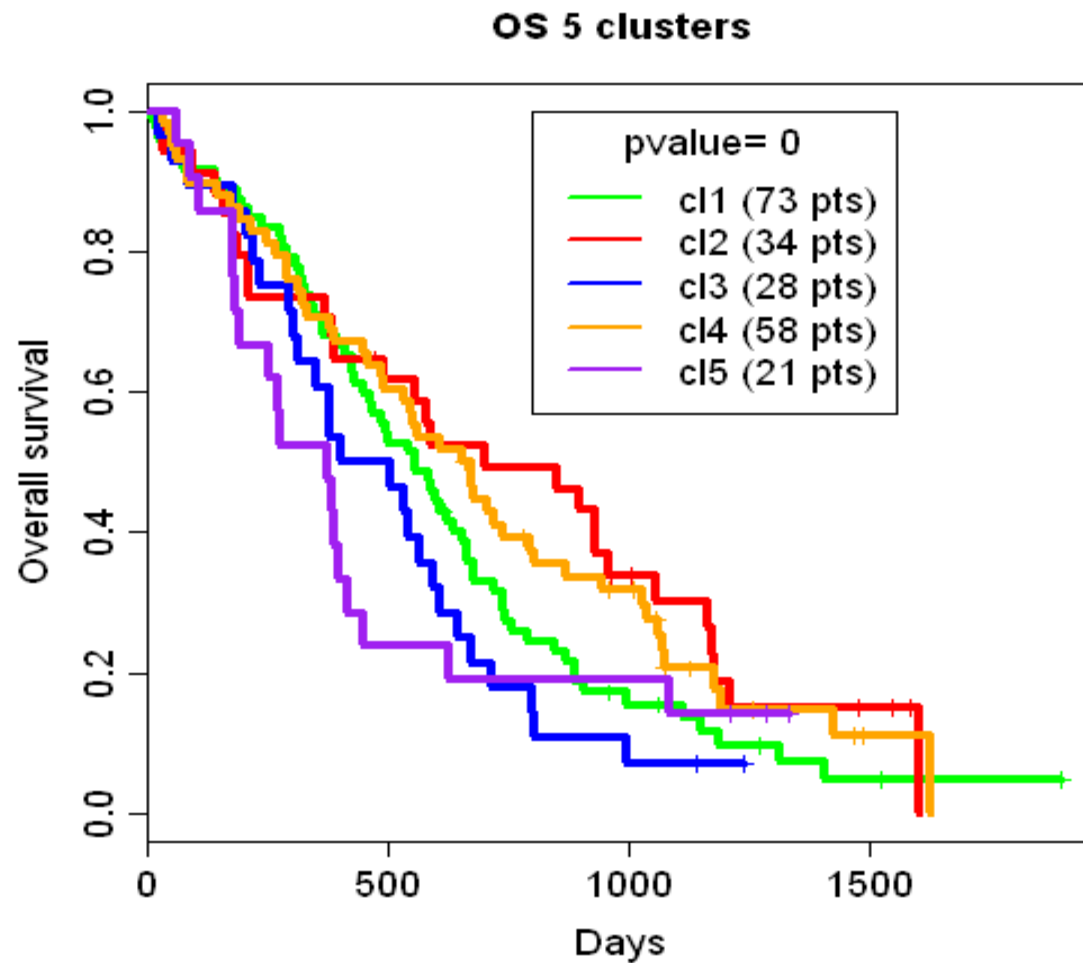
- Clinical annotation
- Biospecimens
 - PALGA = Dutch National Electronic Pathology Archive
 - Nation wide coverage since 1991
 - > 42 million entries
 - > 10 million individuals
 - SNOMED like codes -> structured reports
 - Index to FFPE archives in all 60 labs
 - Rich source of DNA and TMAs

CAIRO 180k arrayCGH on FFPE CRC primary tumor tissue

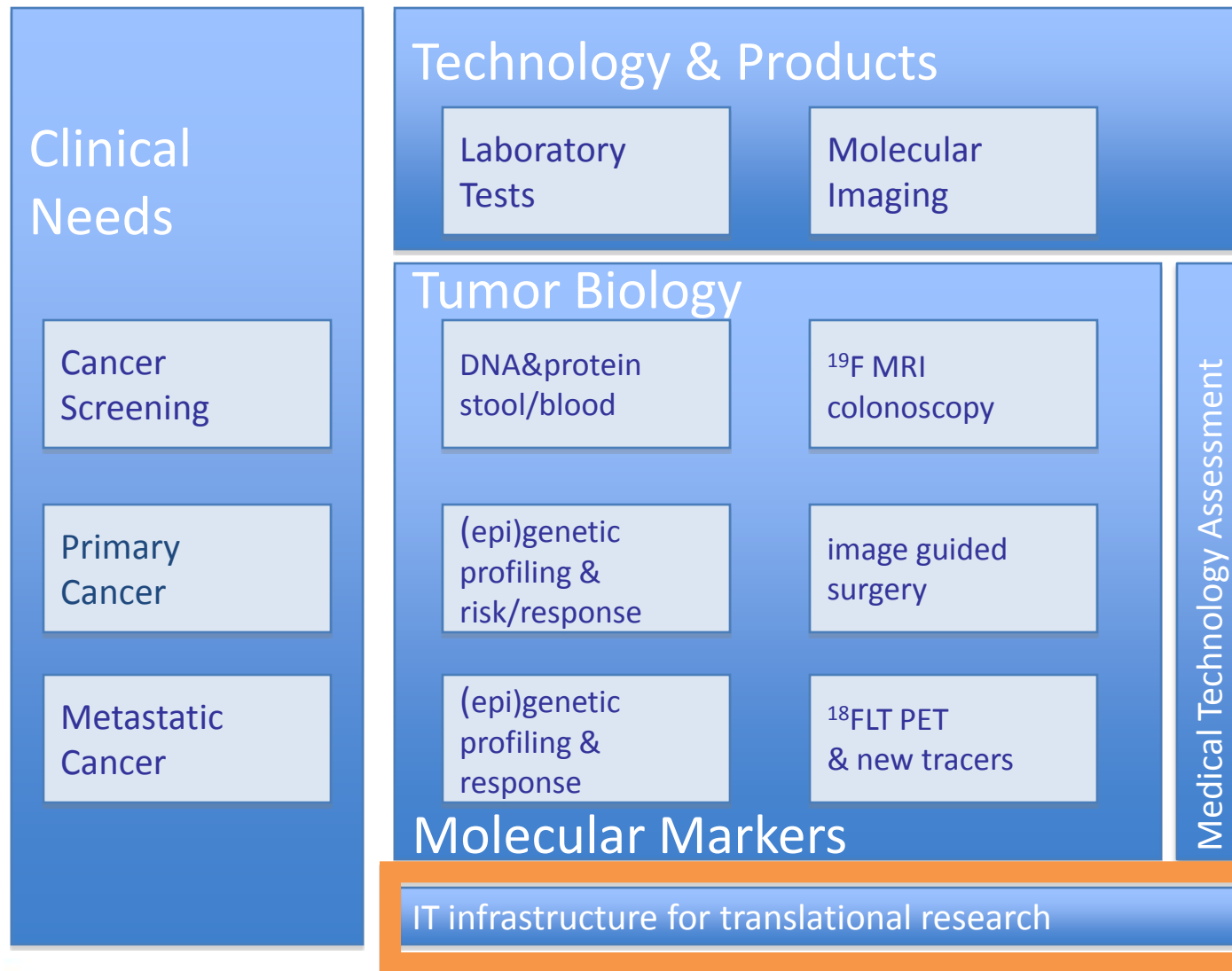




Overall survival



Decrease Colorectal cancer Death

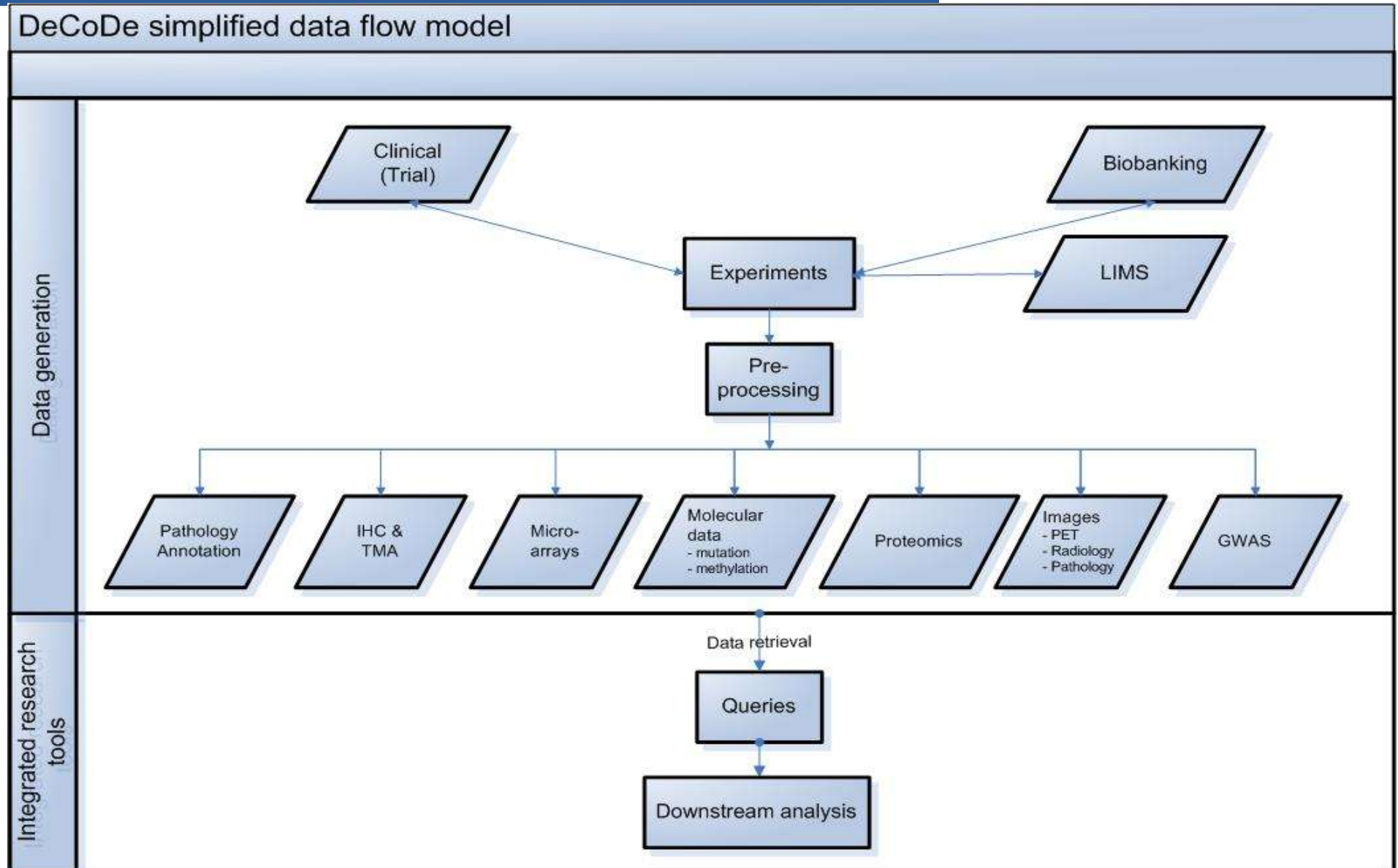




Data management & analysis challenges

- Amount, islands & interoperability
- Linking to other data resources
 - Population registry based invitation systems for cancer screening
 - Retrospective clinical trial data sets
 - National pathology registry
 - String of Pearls biobanking initiative
- Workflow management
 - Data & sample collection
- Storing, integrating and analyzing (including MTA) different types of experimental data
 - Methylation, arrayCGH, proteomics, TMA, images

DeCoDe General flowchart



How did we proceed?

- Summer 2008
 - survey of commercial solutions
- Autumn 2008
 - contact established with caBIG
 - data models compared
- 2009-2010
 - caBIG selected as platform for the DeCoDe consortium
 - several applications implemented/piloted
 - OpenClinica
 - caTissue
 - caArray (pending parser update)
 - caIntegrator
 -

Side effect 1

- CTTM sees caBIG as IT infrastructure of choice
 - caBIG awareness meeting September 2009, Amsterdam
 - Site visit at best practices December 2009, US
- Business plan in preparation for a 15-20 M€ project
 - Implement (adopt/adapt) relevant applications
 - Develop unmet needs/areas of expertise
 - Digital microscopy
 - PET/MRI imaging
 - Other
 - Academic partners: DeCoDe, AirForce, PCMM
 - Private partners: under negotiation
- Time frame
 - Approval October 2010
 - Run time 2011-2014

Side effect 2



VU University Medical Center, Amsterdam

Interconnection

Patient care work flow

Research work flow

Use caBIG for research IT across

- Oncology
- Immunology
- Neurosciences
- Cardiovascular diseases
- Extramural and transmural medicine

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- Jeroen Belien
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String of Pearls

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NBIC

- Barend Mons
- Marc van Driel

Philips

- Henk Obbink

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